

SEQUENCE LISTING



RECEIVED  
JAN 17 2002  
TECH CENTER 1600/2900

<110> HERMONAT, Paul L.

<120> ADENO-ASSOCIATED VIRUS AAV REP78 MAJOR REGULATORY PROTEIN, MUTANTS  
THEREOF AND USES THEREOF

<130> 023533/0130

<140> US 09/693,908

<141> 2000-10-23

<150> US 60/160,608

<151> 1999-10-21

<160> 6

<170> PatentIn version 3.1

<210> 1

<211> 26

<212> DNA

<213> Unknown

<220>

<223> Primer

<400> 1

ccccggaggc cgaattcttt gtgcaa

26

<210> 2

<211> 20

<212> DNA

<213> Unknown

<220>

<223> Primer

<400> 2

acaagcagga ttgaaggcca

20

<210> 3

<211> 20

<212> DNA

<213> Unknown

<220>

<223> Primer

<400> 3

catatcacca gctcaccgtc

20

<210> 4  
 <211> 110  
 <212> DNA  
 <213> Human papillomavirus

<400> 4  
 actacaataa ttcattgtata aaactaaggg cgtaaccgaa atcgggttgaa ccgaaaccgg 60  
 ttagtataaaa agcagacatt ttatgcacca aaagagaact gcaatgtttc 110

<210> 5  
 <211> 4675  
 <212> DNA  
 <213> adeno-associated virus 2

<220>  
 <221> CDS  
 <222> (321)..(2183)  
 <223>

<400> 5  
 ttggccactc cctctctgcg cgctcgctcg ctcaactgagg ccgggcgacc aaaggtcgcc 60  
 cgacgccccg gctttgcccc ggccggcctca gtgagcgagc gagcgcgag agagggagtg 120  
 gccaaactcca tcaactagggg ttcttgagg ggtggagtcg tgacgtgaat tacgtcatag 180  
 ggtaggggag gtctgtatt agaggtcacg tgagtgtttt gcgacatttt gcgacacat 240  
 gtggtcacgc tgggtattta agcccgagtg agcacgcagg gtctccattt tgaagcggga 300  
 ggtttgaacg cgcagccgcc atg ccg ggg ttt tac gag att gtg att aag gtc 353  
 Met Pro Gly Phe Tyr Glu Ile Val Ile Lys Val  
 1 5 10  
 ccc agc gac ctt gac ggg cat ctg ccc ggc att tct gac agc ttt gtg 401  
 Pro Ser Asp Leu Asp Gly His Leu Pro Gly Ile Ser Asp Ser Phe Val  
 15 20 25  
 aac tgg gtg gcc gag aag gaa tgg gag ttg ccg cca gat tct gac atg 449  
 Asn Trp Val Ala Glu Lys Glu Trp Glu Leu Pro Pro Asp Ser Asp Met  
 30 35 40  
 gat ctg aat ctg att gag cag gca ccc ctg acc gtg gcc gag aag ctg 497  
 Asp Leu Asn Leu Ile Glu Gln Ala Pro Leu Thr Val Ala Glu Lys Leu  
 45 50 55  
 cag cgc gac ttt ctg acg gaa tgg cgc cgt gtg agt aag gcc ccg gag 545  
 Gln Arg Asp Phe Leu Thr Glu Trp Arg Arg Val Ser Lys Ala Pro Glu  
 60 65 70 75  
 gcc ctt ttc ttt gtg caa ttt gag aag gga gag agc tac ttc cac atg 593  
 Ala Leu Phe Phe Val Gln Phe Glu Lys Gly Glu Ser Tyr Phe His Met  
 80 85 90

cac gtg ctc gtg gaa acc acc ggg gtg aaa tcc atg gtt ttg gga cgt	641
His Val Leu Val Glu Thr Thr Gly Val Lys Ser Met Val Leu Gly Arg	
95 100 105	
ttc ctg agt cag att cgc gaa aaa ctg att cag aga att tac cgc ggg	689
Phe Leu Ser Gln Ile Arg Glu Lys Leu Ile Gln Arg Ile Tyr Arg Gly	
110 115 120	
atc gag ccg act ttg cca aac tgg ttc gcg gtc aca aag acc aga aat	737
Ile Glu Pro Thr Leu Pro Asn Trp Phe Ala Val Thr Lys Thr Arg Asn	
125 130 135	
ggc gcc gga ggc ggg aac aag gtg gtg gat gag tgc tac atc ccc aat	785
Gly Ala Gly Gly Gly Asn Lys Val Val Asp Glu Cys Tyr Ile Pro Asn	
140 145 150 155	
tac ttg ctc ccc aaa acc cag cct gag ctc cag tgg gcg tgg act aat	833
Tyr Leu Leu Pro Lys Thr Gln Pro Glu Leu Gln Trp Ala Trp Thr Asn	
160 165 170	
atg gaa cag tat tta agc gcc tgt ttg aat ctc acg gag cgt aaa cgg	881
Met Glu Gln Tyr Leu Ser Ala Cys Leu Asn Leu Thr Glu Arg Lys Arg	
175 180 185	
ttg gtg gcg cag cat ctg acg cac gtg tcg cag acg cag gag cag aac	929
Leu Val Ala Gln His Leu Thr His Val Ser Gln Thr Gln Glu Gln Asn	
190 195 200	
aaa gag aat cag aat ccc aat tct gat gcg ccg gtg atc aga tca aaa	977
Lys Glu Asn Gln Asn Pro Asn Ser Asp Ala Pro Val Ile Arg Ser Lys	
205 210 215	
act tca gcc agg tac atg gag ctg gtc ggg tgg ctc gtg gac aag ggg	1025
Thr Ser Ala Arg Tyr Met Glu Leu Val Gly Trp Leu Val Asp Lys Gly	
220 225 230 235	
att acc tcg gag aag cag tgg atc cag gag gac cag gcc tca tac atc	1073
Ile Thr Ser Glu Lys Gln Trp Ile Gln Glu Asp Gln Ala Ser Tyr Ile	
240 245 250	
tcc ttc aat gcg gcc tcc aac tcg cgg tcc caa atc aag gct gcc ttg	1121
Ser Phe Asn Ala Ala Ser Asn Ser Arg Ser Gln Ile Lys Ala Ala Leu	
255 260 265	
gac aat gcg gga aag att atg agc ctg act aaa acc gcc ccc gac tac	1169
Asp Asn Ala Gly Lys Ile Met Ser Leu Thr Lys Thr Ala Pro Asp Tyr	
270 275 280	
ctg gtg ggc cag cag ccc gtg gag gac att tcc agc aat cgg att tat	1217
Leu Val Gly Gln Gln Pro Val Glu Asp Ile Ser Ser Asn Arg Ile Tyr	
285 290 295	
aaa att ttg gaa cta aac ggg tac gat ccc caa tat gcg gct tcc gtc	1265
Lys Ile Leu Glu Leu Asn Gly Tyr Asp Pro Gln Tyr Ala Ala Ser Val	
300 305 310 315	

ttt ctg gga tgg gcc acg aaa aag ttc ggc aag agg aac acc atc tgg	1313
Phe Leu Gly Trp Ala Thr Lys Lys Phe Gly Lys Arg Asn Thr Ile Trp	
320 325 330	
ctg ttt ggg cct gca act acc ggg aag acc aac atc gcg gag gcc ata	1361
Leu Phe Gly Pro Ala Thr Thr Gly Lys Thr Asn Ile Ala Glu Ala Ile	
335 340 345	
gcc cac act gtg ccc ttc tac ggg tgc gta aac tgg acc aat gag aac	1409
Ala His Thr Val Pro Phe Tyr Gly Cys Val Asn Trp Thr Asn Glu Asn	
350 355 360	
ttt ccc ttc aac gac tgt gtc gac aag atg gtg atc tgg tgg gag gag	1457
Phe Pro Phe Asn Asp Cys Val Asp Lys Met Val Ile Trp Trp Glu Glu	
365 370 375	
ggg aag atg acc gcc aag gtc gtg gag tcg gcc aaa gcc att ctc gga	1505
Gly Lys Met Thr Ala Lys Val Val Glu Ser Ala Lys Ala Ile Leu Gly	
380 385 390 395	
gga agc aag gtg cgc gtg gac cag aaa tgc aag tcc tcg gcc cag ata	1553
Gly Ser Lys Val Arg Val Asp Gln Lys Cys Lys Ser Ser Ala Gln Ile	
400 405 410	
gac ccg act ccc gtg atc gtc acc tcc aac acc aac atg tgc gcc gtg	1601
Asp Pro Thr Pro Val Ile Val Thr Ser Asn Thr Asn Met Cys Ala Val	
415 420 425	
att gac ggg aac tca acg acc ttc gaa cac cag cag ccg ttg caa gac	1649
Ile Asp Gly Asn Ser Thr Thr Phe Glu His Gln Gln Pro Leu Gln Asp	
430 435 440	
cgg atg ttc aaa ttt gaa ctc acc cgc cgt ctg gat cat gac ttt ggg	1697
Arg Met Phe Lys Phe Glu Leu Thr Arg Arg Leu Asp His Asp Phe Gly	
445 450 455	
aag gtc acc aag cag gaa gtc aaa gac ttt ttc cgg tgg gca aag gat	1745
Lys Val Thr Lys Gln Glu Val Lys Asp Phe Phe Arg Trp Ala Lys Asp	
460 465 470 475	
cac gtg gtt gag gtg gag cat gaa ttc tac gtc aaa aag ggt gga gcc	1793
His Val Val Glu Val Glu His Glu Phe Tyr Val Lys Lys Gly Gly Ala	
480 485 490	
aag aaa aga ccc gcc ccc agt gac gca gat ata agt gag ccc aaa cgg	1841
Lys Lys Arg Pro Ala Pro Ser Asp Ala Asp Ile Ser Glu Pro Lys Arg	
495 500 505	
gtg cgc gag tca gtt gcg cag cca tcg acg tca gac gcg gaa gct tcg	1889
Val Arg Glu Ser Val Ala Gln Pro Ser Thr Ser Asp Ala Glu Ala Ser	
510 515 520	
atc aac tac gca gac agg tac caa aac aaa tgt tct cgt cac gtg ggc	1937
Ile Asn Tyr Ala Asp Arg Tyr Gln Asn Lys Cys Ser Arg His Val Gly	
525 530 535	

atg aat ctg atg ctg ttt ccc tgc aga caa tgc gag aga atg aat cag	1985
Met Asn Leu Met Leu Phe Pro Cys Arg Gln Cys Glu Arg Met Asn Gln	
540 545 550 555	
aat tca aat atc tgc ttc act cac gga cag aaa gac tgt tta gag tgc	2033
Asn Ser Asn Ile Cys Phe Thr His Gly Gln Lys Asp Cys Leu Glu Cys	
560 565 570	
ttt ccc gtg tca gaa tct caa ccc gtt tct gtc gtc aaa aag gcg tat	2081
Phe Pro Val Ser Glu Ser Gln Pro Val Ser Val Val Lys Lys Ala Tyr	
575 580 585	
cag aaa ctg tgc tac att cat cat atc atg gga aag gtg cca gac gct	2129
Gln Lys Leu Cys Tyr Ile His His Ile Met Gly Lys Val Pro Asp Ala	
590 595 600	
tgc act gcc tgc gat ctg gtc aat gtg gat ttg gat gac tgc atc ttt	2177
Cys Thr Ala Cys Asp Leu Val Asn Val Asp Leu Asp Asp Cys Ile Phe	
605 610 615	
gaa caa taaatgattt aaatcaggta tggctgccga tggttatctt ccagattggc	2233
Glu Gln	
620	
tgcaggacac tctctctgaa ggaataagac agtgggtggaa gctcaaacct ggcccaccac	2293
caccaaagcc cgcagagcgg cataaggacg acagcagggg tcttgtgctt cctgggtaca	2353
agtacctcg acccttcaac ggactcgaca agggagagcc ggtcaacgag gcagacgccg	2413
cggccctcga gcacgtacaa agcctacgac cggcagctcg acagcggaga caaccctac	2473
ctcaagtaca accacgccga cgcggagttt caggagcgcc ttaaagaaga tacgtctttt	2533
gggggcaacc tcggacgagc agtcttccag gcgaaaaaga gggttcttga acctctgggc	2593
ctgggtgagg aacctgttaa gacggctccg ggaaaaaaga ggccggtaga gcactctctt	2653
gtggagccag actcctctc gggaaccgga aaggcggggc agcagcctgc aagaaaaaga	2713
ttgaattttg gtcagactgg agacgcagac tcagtacctg acccccagcc tctcggacag	2773
ccaccagcag cccctctggt tctgggaact aatacgatgg ctacaggcag tggcgacca	2833
atggcagaca ataacgaggg cgccgacgga gtgggtaatt cctccggaaa ttggcattgc	2893
gattccacat ggatgggcga cagagtcac accaccagca cccgaacctg ggccctgccc	2953
acctacaaca accacctcta caaacaatt tccagccaat caggagcctc gaacgacaat	3013
cactactttg gctacagcac cccttggggg tattttgact tcaacagatt cactgccc	3073
ttttcaccac gtgactggca aagactcatc aacaacaact ggggattccg acccaagaga	3133
ctcaacttca agctctttta cattcaagtc aaagaggtca cgcagaatga cggtagcagc	3193

acgattgcc aataaecttac cagcacgggt caggtgttta ctgactcgga gtaccagctc 3253  
 ccgtacgtcc tcggctcggc gcatcaagga tgctcccgcc cgttcccagc agacgtcttc 3313  
 atggtgccac agtatggata cctcaccctg aacaacggga gtcaggcagt aggacgtct 3373  
 tcattttact gcctggagta ctttccttct cagatgctgc gtaccggaaa caactttacc 3433  
 ttcagctaca cttttgagga cgttcctttc cacagcagct acgctcacag ccagagtctg 3493  
 gaccgtctca tgaatcctct catcgaccag tacctgtatt acttgagcag aacaaacact 3553  
 ccaagtggaa ccaccacgca gtcaaggctt cagttttctc aggccggagc gagtgcatt 3613  
 cgggaccagt ctaggaactg gcttcctgga cctgtttacc gccagcagcg agtatcaaag 3673  
 acatctgcgg ataacaacaa cagtgaatac tcgtggactg gagctaccaa gtaccacctc 3733  
 aatggcagag actctctggt gaatccggcc atggcaagcc acaaggacga tgaagaaaag 3793  
 ttttttctc agagcggggg tctcatcttt gggaagcaag gtcagagaa aacaaatgtg 3853  
 aacattgaaa aggtcatgat tacagacgaa gaggaaatcg gaacaaccaa tcccgtggct 3913  
 acggagcagt atggttctgt atctaccaac ctccagagag gcaacagaca agcagctacc 3973  
 gcagatgtca acacacaagg cgttcttcca ggcatgggtc ggcaggacag agatgtgtac 4033  
 cttcaggggc ccatctgggc aaagattcca cacacggacg gacattttca cccctctccc 4093  
 ctcatgggtg gattcggact taaacaccct cctccacaga ttctcatcaa gaacaccccg 4153  
 gtacctgca atccttcgac caccttcagt gcggcaaagt ttgcttctt catcacacag 4213  
 tactccacgg gacacggtca gcgtggagat cgagtgggag ctgcagaagg aaaacagcaa 4273  
 acgctggaat cccgaaattc agtacacttc caactacaac aagtctgtta atcgtggact 4333  
 taccgtggat actaatggcg tgtattcaga gcctcgcccc attggcacca gatacctgac 4393  
 tcgtaatctg taattgcttg ttaatcaata aaccgtttta ttcgtttcag ttgaactttg 4453  
 gtctctgcgt atttctttct tatctagttt ccattggctac gtagataagt agcatggcgg 4513  
 gttaatcatt aactacaagg aacccttagt gatggagttg gccactccct ctctgcgcgc 4573  
 tcgctcgctc actgaggccg ggcgaccaa ggtcgccccg cggccgggct ttgccccggc 4633  
 ggctcagtg agcgagcgag cgcgcagaga gggagtggcc aa 4675

<210> 6  
 <211> 621  
 <212> PRT  
 <213> adeno-associated virus 2

<400> 6

Met Pro Gly Phe Tyr Glu Ile Val Ile Lys Val Pro Ser Asp Leu Asp  
1 5 10 15

Gly His Leu Pro Gly Ile Ser Asp Ser Phe Val Asn Trp Val Ala Glu  
20 25 30

Lys Glu Trp Glu Leu Pro Pro Asp Ser Asp Met Asp Leu Asn Leu Ile  
35 40 45

Glu Gln Ala Pro Leu Thr Val Ala Glu Lys Leu Gln Arg Asp Phe Leu  
50 55 60

Thr Glu Trp Arg Arg Val Ser Lys Ala Pro Glu Ala Leu Phe Phe Val  
65 70 75 80

Gln Phe Glu Lys Gly Glu Ser Tyr Phe His Met His Val Leu Val Glu  
85 90 95

Thr Thr Gly Val Lys Ser Met Val Leu Gly Arg Phe Leu Ser Gln Ile  
100 105 110

Arg Glu Lys Leu Ile Gln Arg Ile Tyr Arg Gly Ile Glu Pro Thr Leu  
115 120 125

Pro Asn Trp Phe Ala Val Thr Lys Thr Arg Asn Gly Ala Gly Gly Gly  
130 135 140

Asn Lys Val Val Asp Glu Cys Tyr Ile Pro Asn Tyr Leu Leu Pro Lys  
145 150 155 160

Thr Gln Pro Glu Leu Gln Trp Ala Trp Thr Asn Met Glu Gln Tyr Leu  
165 170 175

Ser Ala Cys Leu Asn Leu Thr Glu Arg Lys Arg Leu Val Ala Gln His  
180 185 190

Leu Thr His Val Ser Gln Thr Gln Glu Gln Asn Lys Glu Asn Gln Asn  
195 200 205

Pro Asn Ser Asp Ala Pro Val Ile Arg Ser Lys Thr Ser Ala Arg Tyr  
210 215 220

Met Glu Leu Val Gly Trp Leu Val Asp Lys Gly Ile Thr Ser Glu Lys  
225 230 235 240

Gln Trp Ile Gln Glu Asp Gln Ala Ser Tyr Ile Ser Phe Asn Ala Ala  
245 250 255

Ser Asn Ser Arg Ser Gln Ile Lys Ala Ala Leu Asp Asn Ala Gly Lys  
260 265 270

Ile Met Ser Leu Thr Lys Thr Ala Pro Asp Tyr Leu Val Gly Gln Gln  
275 280 285

Pro Val Glu Asp Ile Ser Ser Asn Arg Ile Tyr Lys Ile Leu Glu Leu  
290 295 300

Asn Gly Tyr Asp Pro Gln Tyr Ala Ala Ser Val Phe Leu Gly Trp Ala  
305 310 315 320

Thr Lys Lys Phe Gly Lys Arg Asn Thr Ile Trp Leu Phe Gly Pro Ala  
325 330 335

Thr Thr Gly Lys Thr Asn Ile Ala Glu Ala Ile Ala His Thr Val Pro  
340 345 350

Phe Tyr Gly Cys Val Asn Trp Thr Asn Glu Asn Phe Pro Phe Asn Asp  
355 360 365

Cys Val Asp Lys Met Val Ile Trp Trp Glu Glu Gly Lys Met Thr Ala  
370 375 380

Lys Val Val Glu Ser Ala Lys Ala Ile Leu Gly Gly Ser Lys Val Arg  
385 390 395 400

Val Asp Gln Lys Cys Lys Ser Ser Ala Gln Ile Asp Pro Thr Pro Val  
405 410 415

Ile Val Thr Ser Asn Thr Asn Met Cys Ala Val Ile Asp Gly Asn Ser  
420 425 430



Thr Thr Phe Glu His Gln Gln Pro Leu Gln Asp Arg Met Phe Lys Phe  
435 440 445

Glu Leu Thr Arg Arg Leu Asp His Asp Phe Gly Lys Val Thr Lys Gln  
450 455 460

Glu Val Lys Asp Phe Phe Arg Trp Ala Lys Asp His Val Val Glu Val  
465 470 475 480

Glu His Glu Phe Tyr Val Lys Lys Gly Gly Ala Lys Lys Arg Pro Ala  
485 490 495

Pro Ser Asp Ala Asp Ile Ser Glu Pro Lys Arg Val Arg Glu Ser Val  
500 505 510

Ala Gln Pro Ser Thr Ser Asp Ala Glu Ala Ser Ile Asn Tyr Ala Asp  
515 520 525

Arg Tyr Gln Asn Lys Cys Ser Arg His Val Gly Met Asn Leu Met Leu  
530 535 540

Phe Pro Cys Arg Gln Cys Glu Arg Met Asn Gln Asn Ser Asn Ile Cys  
545 550 555 560

Phe Thr His Gly Gln Lys Asp Cys Leu Glu Cys Phe Pro Val Ser Glu  
565 570 575

Ser Gln Pro Val Ser Val Val Lys Lys Ala Tyr Gln Lys Leu Cys Tyr  
580 585 590

Ile His His Ile Met Gly Lys Val Pro Asp Ala Cys Thr Ala Cys Asp  
595 600 605

Leu Val Asn Val Asp Leu Asp Asp Cys Ile Phe Glu Gln  
610 615 620

44  
9